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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/612,072
Filing Date: July 03, 2003
Appellant(s): LEWIS ET AL.

Stephen G. Baxter

For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 02/25/08 appealing from the Office action mailed 02/15/07.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,129,905	Cutie	10-2000
5,776,433	Tzou et al	07-1998
6,558,651	Riebe et al	05-2003
7,223,381	Lewis et al	05-2007

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11-14, 16-19, 21-26, 28-32, 39-46, 48-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cutie (6,129,905) in view of Tzou et al (5,776,433).

Cutie teaches aerosol formulations for mucosal and/or topical administration containing one or more drugs and a sugar as a dispersant in a pharmaceutically acceptable propellant. Metered dose inhalers suitable for delivering such formulations are also disclosed. Cutie discloses that in an aerosol drug formulation the drug may be **dissolved in the propellant** (col. 1, lines 24-29). In a **solution** formulation, a cosolvent may be added to enhance drug dissolution (col. 2, lines 3-10). The formulations may contain **ethanol** up to 5% of the formulation (col. 5, lines 5-9). It is also disclosed that the formulations may be in a **solution** form and that the sugar acts as a solid diluent/dispersant to aid in the incorporation of the dispersion of **or solubilization** of **actives** and excipients **in hydrocarbon propellants** (see col. 3, lines 59-64). Drugs which may be administered via the said formulations include flunisolide, beclomethasone, triamcinolone, **budesonide** (col. 4, lines 25-35). The said formulations may contain excipients such as antioxidants (col. 5, lines 31-34). The formulations may be filled into conventional aerosol containers using conventional filling equipment well known to those skilled in the art (col. 5, lines 40-45). Examples such as example 5, 7, 8 and 11 show formulations comprising an active agent such as triamcinolone or flunisolide, ethanol and propellant. Cutie lacks disclosure on specific antioxidants such as butylated hydroxyanisole and the canister specifics.

Tzou teaches flunisolide aerosol formulations comprising a therapeutically effective amount of **flunisolide in solution** with ethanol and a propellant selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane and a mixture thereof used for the treatment of bronchial asthma. The formulations may be delivered by a metered dose inhaler with a canister that is inert to flunisolide (see abstract). Tzou discloses that NASALIDE® nasal solution comprises excipients such as butylated hydroxyanisole (col. 1, lines 17-26). It is also disclosed that in the formulations of the invention, the flunisolide is **fully dissolved** and the formulation is free from undissolved flunisolide (col. 2, lines 36-40). Aerosol canisters equipped with conventional valves, preferably metered dose valves (col. 3, lines 45-50). Conventional aerosol canisters can be used to contain a formulation of the invention. The formulations are contained within a glass aerosol vial or an aluminum aerosol vial having an interior formulation chamber coated with a resin that is inert to flunisolide and preferably does not absorb flunisolide from the formulation. Suitable resins for coating the formulation chamber include materials commonly employed as interior can coatings, such as epoxy resins (e.g. epoxy-phenolic resins and epoxy-urea formaldehyde resins).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general formulations of Cutie on solution formulations of corticosteroids, such as budesonide, antioxidants and propellants for inhalation and treatment of respiratory disorders to have looked in the art for specific antioxidants and specific aerosol canisters that would improve stability and efficiency of the inhaled

formulations as taught by Tzou. Furthermore it would have been obvious to a person of ordinary skill in the art to have chosen other antioxidants such as ascorbyl palmitate, since all antioxidants are known and have been used by those skilled in the art.

Claims 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cutie (6,129,905) in view of Tzou et al (5,776,433) as applied to claims 11-14, 16-19, 21-26, 28-32, 39-46, 48-49 above, and further in view of Riebe et al (6,558,651).

Cutie and Tzou, discussed above, lack specific disclosure on the inner surface of the metered dose being composed of anodized aluminum or stainless steel.

Riebe et al teaches aerosol formulations and the suitable canisters for metered dose inhalers. The formulations may be filled into canisters capable of withstanding the vapor pressure of the propellant, such as plastic, plastic-coated glass bottle or preferably a metal can, for example an **aluminum can which may be anodized**, lacquer-coated and/or plastic coated, which container is closed with a metering valve. The MDI can may be a coated metal can such as **aluminum or stainless steel** (see col. 5, lines 20-55).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general formulations of the combined references of Cutie and Tzou on solution formulations of corticosteroids for inhalation and treatment of respiratory disorders filled into conventional metered dose inhalers to have looked in the art for specific aerosol canisters such as coated interiors, that would improve stability and efficiency of the inhaled formulations as taught by Riebe et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 11-14, 16-19, 21-26, 28-32, 35-46, 48 and 49 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 7,223,381 (Application No. 10/244,519). Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims are obvious over the reference claims. Claims 11-14, 16-19, 21-26, 28-32, 35-46, 48 and 49 are drawn to an aerosol formulation comprising budesonide, a propellant vehicle and an antioxidant, wherein the budesonide is dissolved in the propellant. Claims 35-46 are drawn to a pressurized metered dose inhaler comprising the formulation of claim 1 and having specific of the canister. The claims of US Patent No. 7,223,381 are drawn to a pressurized metered dose inhaler containing a pressurized solution aerosol formulation comprising budesonide, a hydrofluorocarbon propellant and a co-solvent in an amount to dissolve or solubilize said budesonide in the mixture of cosolvent and propellant. The difference is that the claims of instant application require an antioxidant, while the claims of '381 do not recite an antioxidant. However, the language of reference claims is the open language of comprising and that it is known in the art that including an antioxidant in such formulations would contribute in stability of the formulations (see Cutie or Tzou et al). Thus one of ordinary skill in the art would have been motivated to have included an antioxidant in the reference claims for improved stability.

(10) Response to Argument

Cutie '905 teaches solutions of active agents such as budesonide, cosolvents such as ethanol, propellants such as HFA 134a and excipients such as antioxidants. A sugar is used as a dispersant or a solubilizing aid. Tzou '433 teaches solutions of flunisolide, ethanol, propellant and discloses specific antioxidants useful for the said solution formulation. Riebe et al teaches the specifics of the device. Thus it is considered that the combination of the three references cited meets all the limitations of the claimed invention.

Appellants primary argument appears to be on the limitation of instant claims "wherein the budesonide is completely dissolved in the propellant vehicle" and that the prior art of record, especially Cutie do not teach the said limitation. Appellant states that while Cutie teaches solutions in the "Background of the Invention" section, the body of the reference teaches dispersions and not solutions. Appellant refers to multiple sections of the Cutie reference to prove that Cutie teaches dispersions and not solutions (see Brief, pages 5-7). The arguments are not found persuasive because 1) Cutie is clearly teaching **solutions for inhalation where the active agents are dissolved in the propellant** and/or a solvent (see "Background of Invention" and col. 3, lines 59-64). 2) It is disclosed that the active agent can be **any one** of those listed in column 4, including budesonide and flunisolid. 3) While the primary concentration of Cutie is on dispersions, it is clearly disclosed that **solutions** can just as successfully and effectively be made and used for inhalations. 4) One of ordinary skill in the art would have obtained adequate teachings from Cutie's disclosure to deduce that solutions of budesonide are

also an option. In other words while Cutie does not exemplify a solution comprising budesonide dissolved in the propellant, it does disclose all the claimed elements and one of ordinary skill in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. *KSR International CO. v. Teleflex Inc.* 82 USPQ 2d 1385 (Supreme Court 2007).

Appellant argues that "there is nothing in Tzou et al which can cure the deficiencies of Cutie". Appellant then continues to state that Tzou et al is completely silent in regard to budesonide (see Brief, page 7). This is not persuasive because, as mentioned above, Cutie does teach solutions where the active agent is dissolved in the propellant, and it teaches that actives can be budesonide or flunioslide, etc. Cutie also discloses that antioxidants can be used in the said formulations. The missing element from Cutie is not the budesonide, but the specific antioxidants. Tzou et al was relied upon for its teachings of specific antioxidants such as butylated hydroxyanisole in solution formulations for inhalation. Tzou et la teach solution formulations of flunisolide. It is noted that flunisolide and budesonide are considered equivalent active agents as they are both steroidal anti-inflammatory agents used in respiratory disorders and both used in inhalation formulations (as disclosed by both Cutie and Riebe et al).

Appellant argues that "Cutie only mentions antioxidants in connection with dispersion formulations, there is no teaching in this reference which would suggest adding an antioxidant to a solution formulation. There is no mention at all of antioxidants in Tzou et al" (see Brief, page 7). This is not persuasive because there is no evidence

that dispersion formulation require different antioxidnats than solution formulations. Appellant has offered no showing or evidence. Mere arguments do not obviate obviousness. 2) Tzou et al **do** teach antioxidants. It is clearly disclosed that nasal solution formulation, NASALIDE®, contains fluniosolide and buylated hydroxyanisole (one of the antioxidants of instant claim 14). Furthermore, while neither references specifically disclose ascorbyl palmitate or tocopherol ester, as the antioxidant, it is known that said antioxidants are functional equivalents (see at least instant claim 14), and one of ordinary skill in the art could have substituted one known antioxidant for another with predictable results.

Appellant argues that "Riebe et al is directed toward powder formulations, not a formulation in which the active agent is dissolved in the propellant" (see Brief, page 8). Appellant continues to argue against Riebe et al because "Riebe et al deals with the specific problem of the adhesion of particulate salbutamol to the walls of the can" (see Brief, page 9). The above arguments are not persuasive because the instant claims are "product claims" and the purpose or intended use limitation is not given patentable weight. Instant claims require a pressurized metered dose inhaler wherein at least a part of the inner surfaces of said pressurized metered dose inhaler is composed of stainless steel (see claim 35) and claim 36 requires the entire inner surface be made of stainless steel. Claim 37 require that at lest a part of the inner surface be composed of anodized aluminum and claim 38 requires entire inner surface be composed of anodized aluminum. Riebe et al disclose that metered dose inhalers are **generally** made of anodized aluminum or stainless steel and may be pre-coated (see col. 5, lines

21-41). While Riebe et al discloses particulate formulations, the device used has to comply with requirements of pressurized delivery and is not restricted to particulate formulations. Furthermore, both Cutie and Tzou et al disclose the solution formulations filled in **conventional** canisters for delivery which are made of metals such as aluminum. Riebe et al was relied on for its specific disclosure of anodized aluminum and stainless steel.

In summary, in response to Appellant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves **or** in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Appellant argues against the Double Patenting rejection of instant claims over claims of '381 patent because "all of the pending claims require the presence of an antioxidant. Quite simply, there is nothing in any of the claims of '381 patent which would suggest an aerosol formulation which contains an antioxidant". This is not persuasive. As stated above, the reference claims use the open language of "comprising" which allows for addition of excipients such as antioxidants. Also one of ordinary skill in the art would have been motivated to include an antioxidant to improve the stability of the formulation.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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